APV by acetylcholine (10 microg/kg/min) injection into mAA. The endothelium-independent vascular function (EIDVF) was determined as a ratio of basal to peak of APV by nitroglycerin (10 microg/kg/min) injection into mAA. Simultaneously, the plasma isoprostane F2alpha-III was measured by ELISA kit (Oxford Biomedical). Results: The infusion of isoprostane F2alpha-III significantly attenuate EDVF in CH rabbits (1.8 ±0.3 vs. 2.3 ±0.1; p<0.01). The treatment by ramatroban can improve the EDVF in CH rabbits (3.8 ±0.2 vs. 2.3 ±0.1; p<0.01). There was no significant difference in the EIDVF among the four groups. The plasma isoprostane F2alpha-III levels in CH or CH + IP rabbits was significant higher than NL rabbits (488 ±44, 858 ±59 vs. 256 ±17 ng/ml,both p<0.01). Conclusion: This study suggested that isoprostane F2alpha III synthesis induced by experimental hypercholesterolemia may be due to impaired endothelial function in rabbits. This effect may be due to TXA2 receptor stimulation.

1155-148 Differential Effects of Cyclooxygenase and Nitric Oxide Inhibition on Endothelium-Dependent Responses in Coronary Arteries From Juvenile and Adult Male Pigs

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Background: Experiments were designed to determine effects of puberty on endothelium-dependent responses in coronary arteries of juvenile and adult males.
Methods: Rings from right coronary artery with and without endothelium from 8 juvenile (2-3 mo; testosterone 67±17 mg/dL) and 8 adult (5-6 mo; testosterone 625±184 mg/dL) male pigs were suspended in organ chambers for measurement of isometric force. During contractions to prostaglandin $F_{2\alpha}$, cumulative concentration response curves to UK-14, 304 (α-adrenergic agonist) and bradykinin (BK) were obtained in the absence and presence of either indomethacin or indomethacin plus N^G-monomethyl-L-arginine (L-NMMA) to inhibit cyclooxygenase and nitric oxide synthase, respectively. Blood was collected for measurement of nitric oxide (NO).
Results: Plasma NO was significantly higher in juvenile compared to adult males (48.7±28.3 vs. 18.6±7.2 µmol/L, p<0.0001). UK-14, 304 caused similar concentration-dependent relaxations only in rings with endothelium from juvenile and adult pigs. With indomethacin, relaxations were significantly enhanced in arteries from adult pigs (EC_{50} = 7.9±0.27 -log mol/L), and reduced in arteries from juvenile pigs (EC_{50} = 6.7±0.37 –log mol/L) (p=0.023). L-NMMA significantly inhibited relaxations in arteries from both groups. Relaxations to BK also were similar in rings with endothelium from juvenile and adult pigs. In arteries from juvenile but not adult pigs, indomethacin caused a rightward shift of the dose response curve (p=0.08). Whereas, L-NMMA in the presence of indomethacin caused significant rightward shift of dose-response curve (p=0.03) in arteries from adult but not juvenile pigs.
Conclusion: Endothelium-dependent responses are selectively modulated by cyclooxygenase and nitric oxide inhibition in coronary arteries from male pigs. At immaturity, inhibition of cyclooxygenase reduces relaxations which is reversed with maturation. Nitric oxide is reduced with maturity and associated with relaxations to BK. Shifts from inhibitory to contractile prostanoids and decreases in plasma NO may be related to production of testosterone.

1155-149 Short-Term Therapy With Gatifloxacin or Azithromycin Prevents the Acceleration of Atherosclerosis After Infection With *Chlamydia Pneumoniae* in a Rabbit Model but Does Not Eradicate the Organism From Plaque

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Background: *Chlamydia pneumoniae* (Cpn) is associated with atherosclerosis in human and animal studies, and short term (<3 months) antibiotic therapy has prevented Cpn-induced atherosclerosis in rabbits. However, short term antibiotic therapy has not demonstrated lasting clinical benefit in recent secondary prevention trials. It is proposed that these poor long-term results may be due to inability of the antibiotic to eradicate the organism. Both azithromycin (A) and gatifloxacin (G) are agents presently being tested for the secondary prevention of atherosclerosis. Whether either is able to eradicate Cpn from atherosclerotic plaque is unknown.
Methods: Forty-five rabbits received a 0.25% dietary supplement of cholesterol and were randomized 2:1 to Cpn infection or placebo and then randomized 1:1:1 to A 30 mg/kg/day X 1 week followed by 30 mg/kg twice weekly for 6 weeks, G 50 mg/kg/day for 7 weeks, or placebo. One uninfected rabbit died spontaneously, and the rest were euthanized 3 months after initial infection. Blinded sections of the aorta were examined to calculate plaque percent area stenosis (PAS) (plaque area / total area within the internal elastic lamina). The presence of Cpn within aortic sections was evaluated by direct immunofluorescence (DIF) (Bartels).
Results: PAS was greater for infected, untreated arteries (39±12%) than the other groups (non-infected = 21±12%; infected + A = 20±11%; infected + G = 22±14%; all p-values <0.05 vs. infected-untreated). DIF was positive within the aortas of 0/14 non-infected, 8/10 infected/untreated, 4/10 infected/A, and 5/10 infected/G rabbits.
Conclusion: Although a seven-week course of A or G significantly prevented Cpn-induced acceleration of atherosclerosis in the rabbit, neither was able to eradicate the organism by three months. This finding may help to explain the disappointing long-term results in recent clinical trials. We propose that longer or different anti-microbial therapy may be required to eradicate Cpn and provide lasting clinical benefit in the setting of primary or secondary prevention for atherosclerosis.

1155-150 Comparison of Effect of Thiazolidinediones on Atherosclerosis in Apolipoprotein E-Deficient Mice

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Background: Thiazolidinediones are peroxisome proliferator-activated receptor-gamma agonists and are used to improve insulin resistance in type II diabetes mellitus. It is controversial whether thiazolidinediones promote or inhibit atherosclerosis in vivo. The purpose of this study is to compare the effect of thiazolidinediones on atherosclerosis in apolipoprotein E (apoE)-deficient mice. **Methods** At 4 weeks of age, male apoE-deficient mice were weaned from mother and fed a powdered F-2 chow diet alone (control group, n=7) or F-2 chow diet with 0.2% troglitazone added (troglitazone group, n=7), with 0.02% pioglitazone added (pioglitazone group, n=7), or with 0.002% rosiglitazone added (rosiglitazone group, n=7). The dose of drugs was determined by the clinical dosage of each drug. At 24 weeks of age, mice were sacrificed and atherosclerotic lesions in the aortic root were measured by a quantitative assay. **Results**: There were no significant differences among 4 groups in body weight, total cholesterol, fasting blood sugar or HbA1c levels at 24 weeks. The atherosclerotic lesion of troglitazone group was significantly smaller than that of control group (control; 0.235±0.052 mm^2 vs. troglitazone; 0.170±0.057 mm^2, p<0.05), in contrast, that of pioglitazone and rosiglitazone groups showed no significant difference compared to control group (pioglitazone; 0.260±0.081 mm^2, rosiglitazone; 0.244±0.058 mm^2). Troglitazone is reported to be a radical-scavenger, because it has a similar structure with vitamin E. Therefore, antioxidant activity was determined by measuring plasma levels of isoprostane (8-epi prostaglandine F2α: 8-epi PGF2α) with gas chromatography-mass spectrometry selected ion monitoring. The plasma 8-epi PGF2α level of the troglitazone group was significantly lower than those of other groups (troglitazone; 186±74 pg/ml vs. control; 353±119, pioglitazone; 410±216, or rosiglitazone; 423±207, p<0.05). **Conclusion**: Troglitazone with accessory antioxidant activity reduces isoprostane generation and the atherosclerosis in apoE-deficient mice, whereas pioglitazone and rosiglitazone do not.

1155-151 The Cardiac Peptide BNP is Superior to ANP and the Renally Derived Peptide Urodilatin in Enhancing Renal Function in Overt Experimental Congestive Heart Failure

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BACKGROUND: Recent studies have reported that improving renal function is the most important predictor of survival in congestive heart failure (CHF). A hallmark of overt CHF is attenuated cGMP production to ANP with renal resistance. BNP is FDA approved for the management of acute CHF and is synthesized and released by cardiomyocytes. Urodilatin (Uro) is from the kidney and has been isolated from human urine with an amino acid (AA) sequence identical to ANP except for N-terminal extension of four AA residues. Studies have reported that exogenous Uro results in greater renal effects as compared to ANP but to date no comparison has been made with BNP nor ANP to BNP. **METHODS:** We determined the cardiorenal and humoral actions of equimolar infusion of (10 pmol/kg/min) ANP (n=6), BNP (n=5) and Uro (n=6) in 3 separate group of dogs with rapid ventricular pacing induced overt CHF (240 bpm for 10 days).**RESULTS:** BNP resulted in increases in urinary sodium excretion (UNaV) (2.2± 0.7 to 164± 76 µEq/min, p<0.05) and glomerular filtration rate (GFR) (27± 4 to 52± 11 ml/min, p=0.05) which were greater as compared to Uro (p<0.05 BNP vs Uro), while ANP did not increase in either UNaV or GFR. The increase in plasma cGMP (25± 2 to 38± 2 pmol/ml, p<0.05) and urinary cGMP excretion with BNP (1618± 151 to 6124± 995 pmol/min, p<0.05) were similar to Uro, however there was no significant change with ANP. Cardiac filling pressures were reduced similarly in all three groups. **CONCLUSION:** In this model of experimental overt CHF, infusion of BNP produced greater increases in UNaV and GFR as compared to Uro, while ANP did not result in significant changes. These favorable renal effects were associated with increases in both plasma cGMP and urinary cGMP excretion, which were similar with BNP and Uro, however were unchanged with ANP. This study demonstrates the superiority of BNP to Uro and ANP in enhancing renal function in severe experimental CHF. These studies also support the conclusion that in CHF, renal resistance to natriuretic peptides in increasing rank order is ANP>Uro>BNP. These results may have clinical implications when considering the therapeutic efficacy of these peptides in the management of overt CHF.

POSTER SESSION

1156 Lipids and Risk Factors

Tuesday, April 01, 2003, 9:00 a.m.-11:00 a.m.
McCormick Place, Hall A
Presentation Hour: 10:00 a.m.-11:00 a.m.

1156-117 Prograf Decreases Plasma Cholesterol in Heart Transplant Recipients With Treated but Persisting Mild Dyslipidemia: The Canadian Multicenter Randomized Trial of Prograf Versus Neoral

Michel White, on behalf of the Canadian Heart Transplantation Group, Montreal Heart Institute, Montreal, PQ, Canada

Background: Despite optimal use of potent lipid-lowering agents, most heart transplant recipients exhibit persisting dyslipidemia not satisfying the current guidelines for high-risk patients. We have initiated a Canadian multicenter prospective study of Neoral mainte-